

The role of Th1 cells in the manifestation of EAE has been widely studied. Th1 but not Th2 cells transfer the disease to normal naive recipients (18). Shifting the Th1/Th2 balance towards Th2 cells by *in vivo* administration of IL-4 (12), by antibodies to B7-1 (14), by soluble peptide therapy (38), or by administration of neutralizing antibodies to IL-12 (15) markedly suppressed EAE.

It has recently been shown that IGIF is a more potent inducer of IFN- $\gamma$  producing Th1 cells than is IL-12 and thus plays an important role in Th1 responses (25). However, the possible role of anti-IGIF immunotherapy in regulation of T cell mediated autoimmunity has never been evaluated.

While reducing the present invention to practice it has been shown, for the first time, that neutralizing antibodies to IGIF ameliorate EAE by shifting the Th1/Th2 balance towards antigen specific Th2 cells.

#### SUMMARY OF THE INVENTION

The present invention disclosed the use of anti interferon gamma inducing factor antibody in the treatment of multiple sclerosis. This use can be effected in a variety of ways as further described and exemplified hereinbelow.

According to one aspect of the present invention there is provided an antibody comprising an immunoglobulin capable of binding interferon gamma inducing factor.

According to another aspect of the present invention there is provided a pharmaceutical composition for inducing protective immunity against multiple sclerosis, comprising a pharmaceutically acceptable carrier and an antibody being capable of binding an interferon gamma inducing factor.

According to still another aspect of the present invention there is provided a pharmaceutical composition for inducing protective immunity against multiple sclerosis, comprising a pharmaceutically acceptable carrier and an interferon gamma inducing factor or an immunogenic portion thereof, thereby eliciting an antibody being capable of binding the interferon gamma inducing factor *in vivo*.

According to an additional aspect of the present invention there is provided a method for treating an animal for inducing protective immunity against multiple sclerosis, the method comprising the step of administering to the animal cells being capable of producing and secreting an antibody

capable of *in vivo* neutralizing an interferon gamma inducing factor in affecting cells to produce interferon gamma.

According to yet additional aspect of the present invention there is provided a method for treating an animal for inducing protective immunity against multiple sclerosis, the method comprising the step of administering to the animal an antibody capable of *in vivo* neutralizing an interferon gamma inducing factor in affecting cells to produce interferon gamma.

According to still additional aspect of the present invention there is provided a method for treating an animal for inducing protective immunity against multiple sclerosis, the method comprising the step of administering to the animal an antigen including an interferon gamma inducing factor or an immunogenic portion thereof, thereby eliciting an antibody being capable of binding *in vivo* an interferon gamma inducing factor.

According to further features in preferred embodiments of the invention described below, the antibody is polyclonal.

According to still further features in the described preferred embodiments the antibody is monoclonal.

According to still further features in the described preferred embodiments the antibody is a neutralizing antibodies to the interferon gamma inducing factor in affecting cells to produce interferon gamma.

According to still further features in the described preferred embodiments the antibody is humanized.

According to another aspect of the present invention there is provided a method for treating an animal for inducing protective immunity against multiple sclerosis, the method comprising the step of administering to the animal a therapeutic composition including a recombinant construct including an isolated nucleic acid sequence encoding a polypeptide being capable of eliciting antibodies capable of *in vivo* neutralizing an interferon gamma inducing factor in affecting cells to produce interferon gamma.

According to yet another aspect of the present invention there is provided a method for treating an animal for inducing protective immunity against multiple sclerosis, the method comprising the steps of (a) removing cells of the animal; (b) genetically modifying the cells *in vitro* with a recombinant construct including an isolated nucleic acid sequence encoding an interferon gamma inducing factor or an immunogenic portion thereof; and (c) reintroducing the genetically modified cells to the animal.

According to still another aspect of the present invention there is provided a pharmaceutical composition for inducing protective immunity

against multiple sclerosis, comprising a pharmaceutically acceptable carrier and a recombinant construct including an isolated nucleic acid sequence encoding a polypeptide being capable of eliciting antibodies capable of *in vivo* neutralizing an interferon gamma inducing factor in affecting cells to produce interferon gamma.

According to further features in preferred embodiments of the invention described below, the nucleic acid sequence being operatively linked to one or more transcription control sequences.

According to still further features in the described preferred embodiments the transcription control sequences are selected from the group consisting of RSV control sequences, CMV control sequences, retroviral LTR sequences, SV-40 control sequences and  $\beta$ -actin control sequences.

According to still further features in the described preferred embodiments the recombinant construct is an eukaryotic expression vector.

According to still further features in the described preferred embodiments the recombinant construct is selected from the group consisting of pcDNA3, pcDNA3.1(+/-), pZeoSV2(+/-), pSecTag2, pDisplay, pEF/myc/cyto, pCMV/myc/cyto, pCR3.1, pCI, pBK-RSV, pBK-CMV, pTRES and their derivatives.

According to still further features in the described preferred embodiments the therapeutic composition is administered to the animal parenterally.

According to still further features in the described preferred embodiments the animal is a human being.

According to still further features in the described preferred embodiments the pharmaceutically acceptable carrier is selected from the group consisting of an aqueous physiologically balanced solution, an artificial lipid-containing substrate, a natural lipid-containing substrate, an oil, an ester, a glycol, a virus and metal particles.

According to still further features in the described preferred embodiments the pharmaceutically acceptable carrier comprises a delivery vehicle that delivers the nucleic acid sequences to the animal.

According to still further features in the described preferred embodiments the delivery vehicle is selected from the group consisting of liposomes, micelles, and cells.

According to still further features in the described preferred embodiments the recombinant construct is an eukaryotic expression vector.